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## SAMPLE SIZE DETERMINATION FOR CLINICAL RESEARCH

Duolao Wang; Ameet Bakhai; Angelo Del Buono; Nicola Maffulli

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Santiago A. Tobar L., Dsc.

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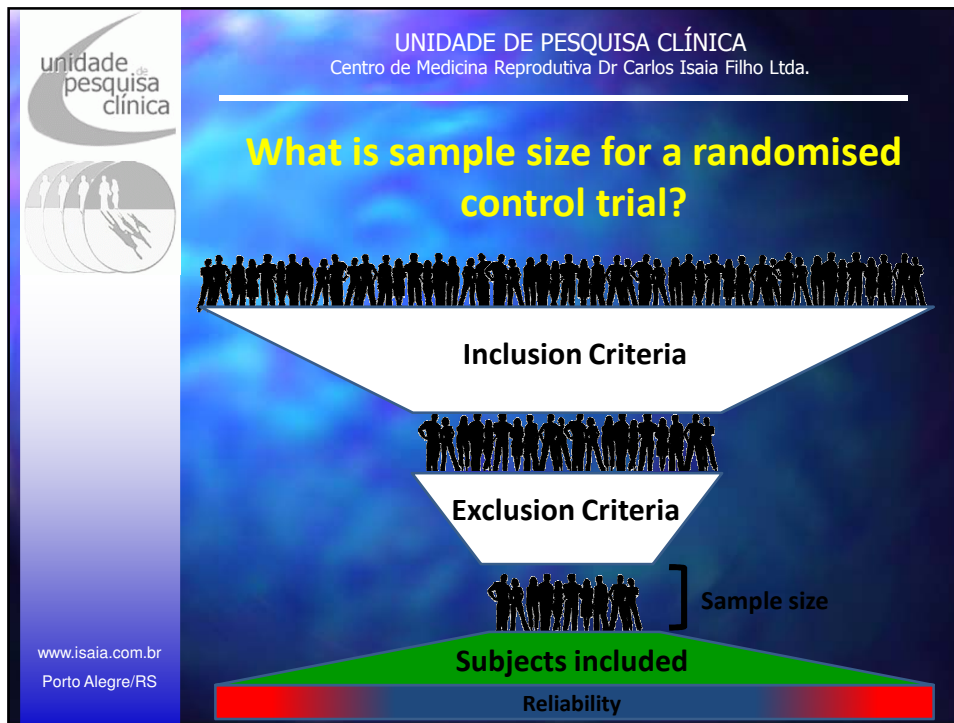
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### Why to determine the sample size?

```
graph LR; Q((Question)) --> A((Answer)); A --> T((True)); A --> F((False)); subgraph Accuracy; T; F; end
```

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*"The major determinant of the reliability of the answer is the sample size of the trial."*



## Results Reliability


**Power to detect (or not) certain magnitude of difference**

*“This number determines the likelihood of being able to detect a certain magnitude of difference (usually an anticipated benefit is assumed) between treatment groups. Either that likelihood or that magnitude can be varied. The likelihood is called the “power” of the study..”*

*“The higher the sample size of patients, the better the power with which to detect a treatment effect, or the smaller the treatment effect that can be detected as significant.*

*Conversely, the lower the sample size the less power with which to detect a treatment effect or the greater the effect must be to be detected as significant.*

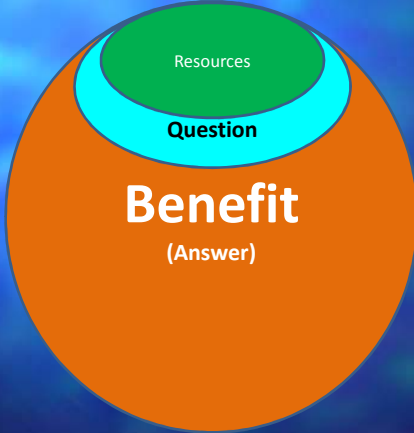
*The sample size calculation is also based on the design of a trial, so how the primary outcome is to be determined must also be clarified in advance of determining sample size.”*



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## Why do we have to choose a sample size?




**Ethical point of view**

“...we cannot wait indefinitely as patients will continue to be given or refused a treatment without evidence.”

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“To create this “fair chance” of capturing such a difference (if it exists) we have to choose a sample size wisely based on realistic initial assumptions.”




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## What factor determine Sample Size?

1. the event rate of patients in the control or standard treatment arm;
2. the smallest treatment effect or benefit to be detected;
3. the significance level at which we reject the null hypothesis of no difference in treatment effects;
4. the power with which we want to detect an effect;
5. the design of the study;
6. the rate of dropouts during the study.



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## Are negative trial due to small sample size?

**NEGATIVE TRIAL = RESULTS ARE NOT STATISTICALLY SIGNIFICANT.**

- Analysis of “Negative” trials have shown that, sometimes investigator assumption lead them to choose a smaller sample size; Which can increase the chance of Error type I (False positive) or Error type II( false negative).



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## So is that It – just apply the formula?

Statisticians have developed various methodologies for determining sample sizes based:

- 1) Number of Treatments;
- 2) Type of Primary endpoint;
- 3) Statistical analysis methods for outcomes and study design

“When determining sample size it is wise to have finalised the main objective of the protocol and then work with a medical statistician to examine a range of assumption...”

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## Conclusions

“The sample size is the most important determinant of statistical power of a study, and a study with inadequate power, unless being conducted as a safety and feasibility study, is unethical.

Sample size calculation is not an exact science and therefore it is important to make realistic and well researched assumptions before choosing an appropriate sample size accounting for dropouts and also including a plan for interim analyses during the study to amend the final sample size”

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## Sample Size Calculation online & Further Readings

<http://ebook.stat.ucla.edu/calculators/powercalc>  
<http://www.dssresearch.com/SampleSize/default.asp>;  
[http://hedwig.mgh.harvard.edu/quant\\_measur/defs.html#cross.](http://hedwig.mgh.harvard.edu/quant_measur/defs.html#cross)

Pocock SJ. Clinical Trials: A Practical Approach. Wiley, New York, 1983.  
Moher D, Dulberg CS, Wells GA. Statistical power, sample size, and their reporting in randomized controlled trials. JAMA 1994; 272:122-124.

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# Thanks!!!

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